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| EXAMINER | |
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| LAU, JONATHAN S | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/578,877 | MAUREL ET AL. | |
| | Examiner | Art Unit | |
| | Jonathan Lau | 4173 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-11 and 13-21* is/are pending in the application.

4a) Of the above claim(s) *17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13-16 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3,pgs/11May2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This application is the national stage entry of PCT/FR04/02912, filed 15 Nov 2004; and claims benefit of foreign priority document FRANCE 0313357, filed 14 Nov 2003.

Claims 1-11 and 13-21 are pending in the current application. Claims 17-20, drawn to non-elected inventions, are withdrawn. Claims 1-11, 13-16 and 21 are examined on the merits herein.

### *Election/Restrictions*

Applicant's election of Group I, claims 1-11, 13-16 and 21, in the reply filed on 19 Dec 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 17-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

The requirement is still deemed proper and is therefore made FINAL.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 14 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 7 recites "Complexes according to claim 1, in which the strontium cation is a dihalogenide, an organic strontium **derivative** or a **complex of strontium with organic solvents**." Claim 14 recites "Complexes according to claim 7, wherein the dihalogenide is a strontium dichloride, sulfate or **hydrate**."

The specification discloses chemicals, such as strontium acetoacetate (specification, page 5, paragraph 18), which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 7 and 14 are directed to encompass derivatives and solvates, which only correspond in some undefined way to specifically instantly disclosed chemicals. None of these derivatives and solvates meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and because chemical derivatives and solvates are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus encompassed by the claim, no description is given as to the structure or composition, such as number of solvent molecules that are present, of the complex of strontium with organic solvents or the hydrate, and no limiting definition of a derivative is disclosed.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought,

he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed derivatives, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the structurally defined chemical compounds, but not the full breadth of the claims, meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See Vas-Cath at page 1115.)

The court of *In re Curtis* held that "a patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when... the evidence indicates ordinary artisans could not predict the operability ... of any other species." (see *In re Curtis* 354 F.3d 1347, 69 USPQ2d 1274, Fed. Cir. 2004). The court of *Noelle v. Lederman* also pointed out that generic claim to anti-CD40CR Mabs lacked written description support because there was no description of anti-human or other species Mabs, and no description of human CD40CR antigen. The court further pointed out that attempt to "define an unknown by its binding affinity to another unknown" failed. See 355 F.3d 1343, 69 USPQ2d 1508, Fed. Cir. 2004.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 10 recites "A method for preparing a medicament intended to stimulate the

production of hematopoietic stem cells, comprising combining the complexes of claim 1 with a pharmaceutically acceptable vehicle, excipient or support."

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: A method for preparing a medicament intended to stimulate the production of hematopoietic stem cells, comprising combining the complexes of claim 1 with a pharmaceutically acceptable vehicle, excipient or support.

The state of the prior art: The prior art teaches that strontium does not increase hematopoietic stem cells in increasing some osteoblasts. See Lymperi et al. (Blood, prepublished online 30 Oct 2007, cited in PTO-892), page 14, lines 13-24.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: Strontium is known to be a bone anabolic agent which enhances osteoblast function and inhibits osteoclast activity. See Lymperi et al. page 4, lines 15-20. However, the complexity of biological systems means that one skilled in the art cannot predict the biological activity for all possible compounds. Therefore the claimed invention is unpredictable.

The Breadth of the claims: The scope of the claims is infinite. Any possible complexes of claim 1 could potentially be used as a medicament intended to stimulate the production of hematopoietic stem cells.

The amount of direction or guidance presented: The specification speaks generally about the correlation between the number of osteoblasts and the number of hematopoietic stem cells. See specification, page 3, lines 6-11. It is suggested that stimulation of osteoblast multiplication by strontium may induce a stimulation of the hematopoietic stem cell niche. See specification, page 3, lines 12-13.

The presence or absence of working examples: The only working examples provided are for the stimulation of bone growth. See instant specification, page 17, lines 4-10.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the biological activity of complexes of claim 1 for the production of hematopoietic stem cells. See MPEP 2164.

The quantity of experimentation necessary: In order to practice the invention for preparing a medicament beyond those known in the art, (such as stimulation of bone growth) one skilled in the art would undertake a novel and extensive research program the biological activity of complexes of claim 1 for the production of hematopoietic stem cells. Because this research would have to be exhaustive, and because it would involve such a wide and unpredictable scope of complexes of claim 1 and biological activities of said complexes, it would constitute an undue and unpredictable experimental burden.

*Genentech*, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims, Applicants fail to provide information sufficient to practice the claimed invention for preparing a medicament intended to stimulate the production of hematopoietic stem cells.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 7 recites, "Complexes according to claim 1, in which the strontium cation is a dihalogenide, an organic strontium derivative or a complex of strontium with organic solvents."

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999).

The term "strontium cation" in claim 7 is used by the claim to mean "strontium cation or strontium salt", while the accepted meaning is "a positively charged ion of

strontium." The term is indefinite because the specification does not clearly redefine the term. See instant specification, page 5, paragraph 18. Claims 14-16 depend from claim 7 and incorporate all limitations therein, including the use of the indefinite term "strontium cation". For consistency, the term "strontium cation" recited in claim 7 has been employed herein to reference both a strontium cation or strontium salt.

The term "dihalogenide" in claim 14 is used by the claim to mean "inorganic strontium compound", while the accepted meaning is "salt comprising two halogen anions." The term is indefinite because the specification does not clearly redefine the term. For consistency, the term "dihalogenide" recited in claim 14 has been employed herein to reference inorganic strontium compounds.

The term "alcoholate" in claim 16 is used by the claim to mean "organic strontium derivative with a metal-oxygen bond", while the accepted meaning is "alkoxide." The term is indefinite because the specification does not clearly redefine the term. For example, claim 16 indicates that strontium ranelate, which is not an acetylacetonate, is considered an alcoholate, when the accepted term for the ranelate is carboxylate, not alkoxide or alcoholate.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11, 13-16 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maurel et al. (US Patent 6,129,924, issued 10 Oct 2000, cited in PTO-892), herein referred to as the '924 Patent, in view of Henquin (Pflugers Archive - European Journal of Physiology, 1980, 383, p123-129, cited in PTO-892).

The '924 Patent discloses organometallic complexes obtainable by the reaction of a cation of metal in the +2 oxidation state useful as a biocatalyst in living metabolism, sitosterol or a plant extract containing sitosterol, and a diglyceride of formula

where $R_1$ is oleic acid and $R_2$ is an oleyl or acetyl group (column 5, lines 13-35), addressing instant claims 1-6, 13 and 21. The '924 Patent discloses the acylgycerol is obtained by isolation from olive oil (column 7, lines 65-67), addressing the product-by-process of instant claim 6. The '924 Patent discloses metal cation in the

form of halides, sulphates, hydrates, acetylacetonates, alkoxides (or alcoholates) or complexes with organic solvents (column 6, lines 9-15), addressing instant claims 7 and 14-16. Instant claim 16 as disclosed claims,

> "Organometallic complexes produced by the process comprising reacting:
> at least one strontium cation,
> sitosterol or a plant extract containing same,
> at least one mono-, one di- or one triglyceride corresponding to formula (I): in which: $R_1$ is an acyl moiety of a C14 to C24 fatty acid, saturated or not, linear or branched, a hydrogen atom, or a mono-, di- or tri-galactose or glucose, $R_2$ is an acyl moiety of a C2 to C 18 fatty acid, linear or branched, saturated or not, $R_3$ is an acyl moiety of a C14 to C24 fatty acid, saturated or not, linear or branched, or a hydrogen atom,
> **in which the strontium cation is a dihalogenide, an organic strontium derivative or a complex of strontium with organic solvents,**
> wherein the organic strontium derivative is an acetylacetonate or an alcoholate,
> wherein the organic strontium derivative is strontium ranelate."

Instant claim 16 does not require that the strontium cation is an organic strontium derivative. Therefore an organometallic complex in which the metal cation is the dihalogenide in the form of a metal halide addresses instant claim 16. The '924 Patent discloses pharmaceutical compositions comprising said organometallic complex and a pharmaceutically acceptable vehicle, excipient, or carrier (column 10, lines 16-19), addressing instant claim 8. The '924 Patent discloses preparation of a medicine of said organometallic complex such as said pharmaceutical composition (column 10, lines 47-49), addressing instant claims 9 and 10. The '924 Patent discloses "A method for preparing a medicament comprising combining the complexes of claim 1 with a pharmaceutically acceptable vehicle, excipient or support", therefore the disclosed invention addresses all structural limitations of instant claims 9 and 10. See MPEP 2111.02 II. The '924 Patent discloses dietary products that contain said organometallic complex (column 11, lines 11-12), addressing instant claim 11. The '924 Patent discloses the organometallic complex useful as a product with anti-diabetic and/or

insulinomimetic activity and that the choice of the metal cation will be based on the desired activity (column 5, lines 44-48).

The '924 Patent does not disclose the specific cation of metal in the +2 oxidation state, strontium.

Henquin teaches that strontium ions in the +2 oxidation state supports glucose-stimulated insulin release (page 127, right column, lines 27-29). Henquin teaches $Sr^{2+}$ is active in the insulin releasing process but does not have the same efficiency as $Ca^{2+}$ (page 128, right column, lines 41-48).

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the cation of metal in the +2 oxidation state of the organometallic complexes disclosed in the '924 Patent with strontium ions in the +2 oxidation state taught by Henquin. Both the the organometallic complexes disclosed in the '924 Patent and strontium ions in the +2 oxidation state taught by Henquin have anti-diabetic and/or insulinomimetic activity. Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute equivalents known for the same purpose. See MPEP 2144.06. The fact that Henquin teaches $Sr^{2+}$ does not have the same insulin releasing efficiency as $Ca^{2+}$ does not consititute teaching away from the broader disclosure of $Sr^{2+}$ as a cation of metal in the +2 oxidation state with anti-diabetic and/or insulinomimetic activity. See MPEP 2123 II.

Claims 1-11, 13-16 recite a product-by-process. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its

method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) (Claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.). See MPEP 2113.

***Conclusion***

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Ardin Marschel can be reached on 571-272-0718 or Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSL

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